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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/758,773	01/16/2004	Seng H. Cheng	07680.0018	6298
22852	7590	09/26/2008		
FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER LLP 901 NEW YORK AVENUE, NW WASHINGTON, DC 20001-4413				
			EXAMINER	
			CHEN, SHIN LIN	
			ART UNIT	PAPER NUMBER
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

### Office Action Summary

**Application No.**

10/758,773

**Applicant(s)**

CHENG ET AL.

**Examiner**

Shin-Lin Chen

**Art Unit**

1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 12 August 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1, 3, 4, 6-12, 14-18, 20, 22, 36-38 and 40-47 is/are pending in the application.
- 4a) Of the above claim(s) 10-12, 22 and 42-47 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1, 3, 4, 6-9, 14-18, 20, 36-38, 40 and 41 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-848)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

### **DETAILED ACTION**

Upon further consideration of the instant application, the finality of rejection of the last Office action is withdrawn. Action of merit follows.

The amendment filed 8-12-08 has been entered. Claims 1, 8, 22 and 38 have been amended. Claims 1, 3, 4, 6-12, 14-18, 20, 22, 36-38 and 40-47 are pending.

It should be noted that the subject matter of “a method of treating a subject having a lysosomal disease, such as Fabry disease, comprising administering a gene therapy vector under the control of a tissue specific regulatory element and an exogenously produced natural or recombinant lysosomal hydrolase, such as alpha-galactosidase.” is considered in the instant invention in view of the election filed 8-3-06. The phrase “such as Fabry disease” is meant by Examiner that Fabry disease is the sole lysosomal disease to be considered. Therefore, only a method of treating Fabry disease by combining gene therapy and enzyme therapy is considered at this time. Thus, claims 42-46 will NOT be considered at this time.

Claims 1, 3, 4, 6-9, 14-18, 20, 36-38, 40 and 41 are under consideration. Claims 42-46, which are added in the amendment filed 12-3-07, were inadvertently included in the considered claims. The claims are directed to Niemann-Pick disease and Gaucher disease. As discussed above, the intended disease to be considered in elected group I is Fabry disease. Therefore, claims 42-46 will not be considered at this time and they could be rejoined in order when the claims directed to Fabry disease are found allowable.

***Priority***

Application No. 09/884,526, filed 6-19-01, failed to disclose the subject matter of using tissue-specific promoter or liver-specific promoter (independent claim 1) or using human albumin promoter and human prothrombin enhancer (independent claim 20) in gene therapy vector for treating Fabry disease. Therefore, the priority dates of 09/884,526 and 60/212,377 are NOT granted. The effective priority date of the instant invention is the filing date of the invention, i.e. 1-16-04.

***Claim Rejections - 35 USC § 112***

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1, 3, 4, 6, 7, 9, 14-18, 20, 36, 37, 40 and 41 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for reducing the level of globotriaosylceramide (Gb3) in a patient with Fabry disease by infusing an AAV vector expressing alpha-galactosidase A protein under the control of liver-specific promoter in combination with infusing a recombinant alpha-galactosidase A protein to said patient, does not reasonably provide enablement for treating a subject having Fabry disease by first administering a gene therapy vector expressing alpha-galactosidase A protein under the control of a liver-specific regulatory element and then administering natural or recombinant alpha-galactosidase A protein so as to provide therapeutic effect for treating Fabry disease in vivo and the pathological symptoms of Fabry disease have been ameliorated or eliminated. The specification does not

enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

While determining whether a specification is enabling, one considered whether the claimed invention provides sufficient guidance to make and use the claimed invention, if not, whether an artisan would have required undue experimentation to make and use the claimed invention and whether working examples have been provided. When determining whether a specification meets the enablement requirement, some of the factors that need to be analyzed are: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill, the level of predictability in the art, the amount of direction provided by the inventor, the existence of working examples, and whether the quantity of any necessary experimentation to make or use the invention based on the content of the disclosure is “undue” (In re Wands, 858 F.2d at 737, 8 USPQ2d 1400, 1404 (Fed. Cir.1988)).

Furthermore, the USPTO does not have laboratory facilities to test if an invention with function as claimed when working examples are not disclosed in the specification, therefore, enablement issues are raised and discussed based on the state of knowledge pertinent to an art at the time of the invention, therefore skepticism raised in the enablement rejections are those raised in the art by artisans of expertise.

The claims are directed to a method of treating a subject having a Fabry disease by first administering a gene therapy vector, such as an AAV vector, encoding a lysosomal hydrolase protein under the control of at least one tissue specific regulatory element, such as a liver specific promoter or a tissue specific enhancer, and then administering an exogenously produced natural or recombinant lysosomal hydrolase protein or a method of treating a subject having Fabry

disease comprising first administering a gene therapy vector encoding alpha-galactosidase A under the control of a human albumin promoter and 2 copies of a human prothrombin enhancer and then administering an exogenously produced natural or recombinant alpha-galactosidase A, wherein the lysosomal hydrolase is one that is deficient in the subject. Claims 6 and 37 specify a lesser amount of natural or recombinant lysosomal hydrolase is administered than would be administered if the subject had not been administered a gene therapy vector encoding a lysosomal hydrolase or had been administered a gene therapy vector without a tissue specific promoter.

The specification discloses generation of adeno-associated viral vector AAV2/CMVHI-alphagal expressing human alpha-galactosidase under the control of CMV promoter/enhancer and vector AAV2/DC190-alphagal expressing human alpha-galactosidase under the control of human serum albumin promoter and 2 copies of the human prothrombin enhancer (e.g. Example 2). Administration of AAV2/CMVHI-alphagal into immunosuppressed mice via the tail vein results in expression of alpha-galactosidase in liver, hearts and spleens and reduction of accumulated GL-3 level in those organs but none in the kidney. Administration of AAV2/DC-190-alphagal into immuno-competent mice (BALB/c) via tail vein results in 2 to 3 logs higher expression of alpha-galactosidase in those organs, including kidney (Examples 4-6). The use of liver-specific promoter/enhancer DC190 results in a reduced host immune response to the encoded human alpha-galactosidase in the AAV2/DC-190-alphagal-treated mice and sustained expression levels of the enzyme (Examples 7-8). Basal levels of GL-3 in the liver, heart and spleen were attained in Fabry mice treated with systemic administration of AAV2/DC-190-alphagal vector and about 40% reduction in substrate levels in the kidney was also achieved

(Example 9). The claims encompass treatment of a subject having Fabry disease comprising first administering any gene therapy vector encoding alpha-galactosidase A under the control of at least one liver-specific regulatory element or under the control of human albumin promoter and 2 copies of a human prothrombin enhancer and then administering an exogenously produced natural or recombinant alpha-galactosidase A via various administration routes. Here, it is assumed that the lysosomal hydrolase that is deficient in Fabry disease patient is alpha-galactosidase A.

The specification fails to provide adequate guidance and evidence for how to treat a subject having Fabry disease comprising first administering any gene therapy vector encoding alpha-galactosidase A under the control of at least one liver-specific regulatory element or under the control of a human albumin promoter and 2 copies of a human prothrombin enhancer and then administering an exogenously produced natural or recombinant alpha-galactosidase A via various administration routes so as to provide therapeutic effect and to ameliorate the pathological symptoms of the diseases.

The state of the art of treating Fabry disease either via gene therapy or enzyme replacement therapy only demonstrates that the Gb3 level is reduced. Schiffmann et al., January 2000 (PNAS, Vol. 97, No. 1, p. 365-370) teaches i.v. infusion of purified alpha-galactosidase A (alpha-gal A) enzyme into patient results in distribution of the enzyme in several cell types, including sinusoidal endothelial cells, Kupffer cells, and hepatocytes, and Gb3 levels are significantly reduced in the liver and shed renal tubular epithelial cells in the urine sediment. Ziegler et al., 1999 (Human Gene Therapy, Vol. 10, p. 1667-1682) shows that intravenous injection of Ad2/CMVH1alpha-Gal into Fabry knockout mice results in elevation of alpha-

galactosidase in all tissues and a significant reduction in GL-3 level in all tissues to near normal levels for up to 6 months posttreatment (e.g. abstract). However, the various pathological symptoms of Fabry disease of the patient have not been reported to be ameliorated through either gene therapy or enzyme replacement therapy or combination of those two therapies. Bongiorno et al., 2003 (JEADV, Vol. 17, p. 676-679) reports that "Fabry disease is a multisystem disorder associated with wide variety in clinical expression. Fabry disease is an X-linked lysosomal storage disorder caused by a deficiency of alpha-galactosidase A. The enzyme defect leads to the systemic accumulation of glycosphingolipids with alpha-galactosyl moieties consisting predominantly of globotriaosylceramide, galabiosylceramide and two additional glycosphingolipids" (e.g. abstract). Masson et al., 2004 (Joint Bone Spine, Vol. 71, p. 381-383) discloses that in males having Fabry disease, severe multisystem disease develops in childhood or adolescence. "Attacks of acute pain lasting a few minutes to a few days occur in the hands and feet, joints, muscles, and abdomen, sometimes with fever. Highly suggestive skin lesions called angiokeratomas develop, as well as cornea verticillata characterized by corneal deposits without visual impairment. Stroke, seizures, heart disorders (conduction disturbances, valve disease, and left heart failure) and kidney disorders (proteinuria and chronic, renal failure) develop in the third or fourth decade of life. Women...may have moderate or severe disease related to uneven chromosome X inactivation. Late-onset variants with predominant neurological, cardiac, or renal manifestations have been described" (e.g. abstract). It appears that Fabry disease is a multisystem disorder associated with wide variety in clinical expression and the pathological symptoms of Fabry disease are very complicated and can vary from males to



females, and from childhood to adolescence. Gb3 is not the only substrate that accumulates in the patient having the Fabry disease.

Wraith, J.E., 2006 (J. of inherit. Metab. Dis., Vol. 29, p. 442-447) reports that there is an inability to target the infused enzymes to specific sites of pathology, especially the central nervous system and a lack of suitable animal models of the human disease in which to evaluate the new therapy (intravenous infusion of lysosomal enzymes) (e.g. p. 442, right column). Eto et al., 2004 (J. Inherit. Metab. Dis., Vol. 27, p. 411-415) also points out that “[m]ost lysosomal storage diseases have central nervous system (CNS) involvement. No effective treatment is available at present” (e.g. p. 411, Summary). Further, there is no correlation between reduction of GL-3 level in the organs and treatment of Fabry disease in a subject, i.e. amelioration of pathological symptoms of Fabry disease in vivo. Reduction of GL-3 in organs in a subject does not necessarily mean that the Fabry disease is treated. As discussed above, the pathological symptoms of Fabry disease are very complicated and accumulation of glycosphingolipids with alpha-galactosyl moieties consisting of galabiosylceramide and two additional glycosphingolipids are also involved in Fabry disease, and there is no evidence of record that shows reduction of GB3 would result in amelioration of various pathological symptoms of Fabry disease in vivo. Absent specific guidance and evidence, one skilled in the art at the time of the invention would not know how to treat Fabry disease with combination of gene therapy and enzyme therapy such that therapeutic effect can be obtained and pathological symptoms can be ameliorated in vivo.

For the reasons discussed above, it would have required undue experimentation for one skilled in the art at the time of the invention to practice over the full scope of the invention

claimed. This is particularly true given the nature of the invention, the state of the prior art, the breadth of the claims, the amount of experimentation necessary, the level of ordinary skill which is high, the working examples provided and scarcity of guidance in the specification, and the unpredictable nature of the art.

Applicants argue that alpha-galactosidase has been used commercially for treating Fabry disease. FDA has approved numerous lysosomal hydrolases for enzyme replacement therapy including glucocerebrosidase for Gaucher's disease and alpha-galactosidase for Fabry disease etc. Applicants argue that treating a lysosomal disease does not require that all of the diverse pathological symptoms be ameliorated so long as there is some benefit from the treatment (Amendment, p. 9-18). This is not found persuasive because of the reasons set forth above under 35 U.S.C. 112 first paragraph. There are numerous pathological symptoms of Fabry disease including acute pain lasting a few minutes to a few days occur in the hands and feet, joints, muscles, and abdomen, sometimes with fever, skin lesions called angiokeratomas, cornea verticillata, stroke, seizures, heart disorders (conduction disturbances, valve disease, and left heart failure) and kidney disorders (proteinurea and chronic, renal failure), and neurological, cardiac, or renal manifestations. The state of the art of treating Fabry disease either via gene therapy or enzyme replacement therapy only demonstrates that the Gb3 level is reduced. However, the various pathological symptoms of Fabry disease of the patient have not been reported to be ameliorated through either gene therapy or enzyme replacement therapy or combination of those two therapies. Further, there is no correlation between reduction of GL-3 level in the organs and treatment of Fabry disease in a subject, i.e. amelioration of pathological

symptoms of Fabry disease in vivo. Reduction of GL-3 in organs in a subject does not necessarily mean that the Fabry disease is treated.

Applicants argue that clinical pathology of lysosomal storage diseases is caused by build-up of the substrate for the deficient lysosomal hydrolase and the accumulated substrate is responsible for the damage to cells and results in the pathology of the lysosomal diseases. Applicants cite reference Wraith and argue that the first goal of an LSD treatment is to reduce the level of storage metabolite within the cells or organs of the individual and reduction of GL-3 is the primary efficacy endpoint (amendment, p. 18-22). This is not found persuasive because of the reasons set forth above under 35 U.S.C. 112 first paragraph. The pathological consequences of Fabry disease or other LSD are the result of deficiency of alpha-galactosidase or other corresponding enzyme and the accumulation of particular storage metabolite. However, the cells or organs that are affected by the accumulated metabolite are not limited to the primary organ, such as liver for Fabry disease. There are numerous pathological symptoms of Fabry disease including acute pain lasting a few minutes to a few days occur in the hands and feet, joints, muscles, and abdomen, sometimes with fever, skin lesions called angiokeratomas, cornea verticillata, stroke, seizures, heart disorders (conduction disturbances, valve disease, and left heart failure) and kidney disorders (proteinurea and chronic, renal failure), and neurological, cardiac, or renal manifestations. Organs or tissues like hand, joint, muscles, central nervous system, cornea, skin, heart and kidney etc., can be affected in Fabry disease. However, there is no evidence of record that shows administration of gene therapy vector and enzyme to liver or reduction of GL-3 level would be able to ameliorate any of the pathological symptoms in various

organs or tissues in the patient. A first goal or primary efficacy endpoint does not mean the pathological symptoms of the Fabry disease are ameliorated in the patient.

Applicants cite various documents regarding methods for performing gene therapy (amendment, p. 23-26). This is not found persuasive because of the reasons set forth above under 35 U.S.C. 112 first paragraph. Each gene therapy protocol has to be considered separately. The success in one gene therapy cannot be extrapolated into success in other gene therapy. The cited references do not render success in treating Fabry disease by combining gene therapy and enzyme therapy to ameliorate various pathological symptoms in a patient.

*Claim Rejections - 35 USC § 103*

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

4. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 1, 3, 7-9, 14-18, 20, 38, 40 and 41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schiffmann et al., January 2000 (PNAS, Vol. 97, No. 1, p. 365-370) and Ziegler et al., 1999 (Human Gene Therapy, Vol. 10, p. 1667-1682) in view of Demaris et al., 2006 (US Patent No. 7,090,836 B2) and Souza et al., 2007 (US Patent No. 7,312,324 B2).

The claims are directed to a method of treating a subject having a Fabry disease by first administering a gene therapy vector, such as an AAV vector, encoding a lysosomal hydrolase protein under the control of at least one tissue specific regulatory element, such as a liver specific promoter or a tissue specific enhancer, and then administering an exogenously produced natural or recombinant lysosomal hydrolase protein or a method of treating a subject having Fabry disease comprising first administering a gene therapy vector encoding alpha-galactosidase A under the control of a human albumin promoter and 2 copies of a human prothrombin enhancer and then administering an exogenously produced natural or recombinant alpha-galactosidase A, wherein the lysosomal hydrolase is one that is deficient in the subject. Claims 8 and 38 specify the treatment results in a decrease in GL-3 in the subject compared to the GL-3 level in the untreated subject. Claims 14 and 40 specify the viral vector is AAV1, AAV2, AAV5, AAV7 or AAV8. Claim 41 specifies the liver-specific regulatory element is DC190 (a human albumin promoter and 2 copies of a human prothrombin enhancer).

Schiffmann et al., January 2000 (PNAS, Vol. 97, No. 1, p. 365-370) teaches i.v. infusion of purified alpha-galactosidase A (alpha-gal A) enzyme into patient results in distribution of the enzyme in several cell types, including sinusoidal endothelial cells, Kupffer cells, and hepatocytes, and globotriaosylceramide (Gb3) levels are significantly reduced in the liver and shed renal tubular epithelial cells in the urine sediment.

Ziegler et al., 1999 (Human Gene Therapy, Vol. 10, p. 1667-1682) shows that intravenous injection of Ad2/CMVH1alpha-Gal into Fabry knockout mice results in elevation of alpha-galactosidase in all tissues and a significant reduction in GL-3 level in all tissues to near normal levels for up to 6 months posttreatment (e.g. abstract).

Schiffmann and Ziegler do not specifically teach using liver specific regulatory sequence, such as DC190, in gene therapy vector or combination of gene therapy and enzyme therapy.

Desmaris teaches treating MPS I patient with gene therapy in combination with enzyme replacement therapy (e.g. column 5, lines 50-53).

Souza teaches combining promoter elements that have the potential to direct effective and sustained expression with liver specific enhancer element to achieve high and sustained transgene expression in liver. The promoter elements include human serum albumin promoter and alpha-1-antitrypsin promoter, and the enhancer elements include HAS enhancers, a human prothrombin enhancer and an alpha-1-microglobulin enhancer (e.g. column 6, 2<sup>nd</sup> full paragraph). Souza also teaches a DNA vector comprising a human serum albumin promoter and two human prothrombin enhancers (e.g. claim1).

It would have been prima facie obvious for one of ordinary skill in the art at the time of the invention to combine gene therapy and enzyme therapy in treating Fabry disease because Desmaris teaches combining gene therapy and enzyme therapy in treating MPS I, which is also a lysosomal storage disease. Administering gene therapy vector first and then administering enzyme in treating Fabry disease would be obvious to one of ordinary skill because determining the order of administering gene therapy vector and enzyme would be routine optimization in order to obtain the most effective procedure to treat Fabry disease. It also would have been

prima facie obvious to one of ordinary skill in the art to use liver specific regulatory elements in gene therapy vector because Souza teaches using liver specific promoter, such as human serum albumin promoter, and liver specific enhancer, such as human prothrombin enhancer, to achieve high and sustained transgene expression in liver and it was known the primary target tissue in treating Fabry disease is liver.

One having ordinary skill in the art at the time of the invention would have been motivated to do so in order to reduce the level of GL-3 (or Gb3) in Fabry disease patient as taught by Schiffmann and Ziegler with reasonable expectation of success.

### *Conclusion*

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shin-Lin Chen whose telephone number is (571) 272-0726. The examiner can normally be reached on Monday to Friday from 9:30 am to 6 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571) 272-4517. The fax phone number for this group is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is

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(866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Shin-Lin Chen, Ph.D.

/Shin-Lin Chen/

Primary Examiner, Art Unit 1632